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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/030,485 | 06/17/2002 | Ma Clara Blaines Mira | 11279/3 | 6439 |

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| EXAMINER |
|---|
| KAM, CHIH MIN |

Brinks Hofer
Gilson & Lione
PO Box 10395
Chicago, IL 60610

| ART UNIT | PAPER NUMBER |
|---|---|
| 1653 | |

DATE MAILED: 03/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/030,485 | MIRA ET AL. | |
| | Examiner | Art Unit | |
| | Chih-Min Kam | 1653 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *23 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *6-10 and 20-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,11,12 and 15* is/are rejected.

7)☒ Claim(s) *13, 14, 16-19 and 23* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/20/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election of Group I, claims 1-5, 11-19 and 23 without traverse in the Response to the restriction requirement filed January 23, 2004 is acknowledged.

### *Oath/Declaration*

2. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02. The oath or declaration is defective because the priority documents PCT/ES00/00058, which is not a foreign document, is listed in the section of claiming foreign priority under 35 U.S.C. 119 (a)-(d).

### *Claim Objections*

3. Claims 1-5, 11-19 and 23 are objected to because of the use of "SEQ.ID.NO.". Use of "SEQ ID NO:" is suggested.

4. Claim 12 is objected to because of the use of the term "A mixture according to claim 11". Since claim 12 is dependent from claim 11, the term "The mixture according to claim 11".

### *Claim Rejections - 35 USC § 101*

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 1-5, 11 and 12 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claim is drawn to a peptide or a

peptide mixture. As written, the claim does not explicitly indicate the hand of man. Insertion of "isolated" or "synthetic" in connection with a peptide or peptides is suggested. See MPEP § 2105.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 5 is rejected under 35 U.S.C. 112, first paragraph because the specification, while being enabling for a peptide of SEQ ID NO:2 or 3 having esterification of the carboxyl group on Glu or Asp residue that increases its bioavailability and facilitates its permeation through the blood brain barrier and epithelia tissue, does not reasonably provide enablement for a peptide having an amino acid sequence of SEQ ID NO:2 or 3 comprising a reversible modification that increases its bioavailability and facilitates its permeation through the blood brain barrier and epithelia tissue, where the reversible modification is not defined, and the product of the modification is not identified. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claim 5 encompasses a peptide having an amino acid sequence of SEQ ID NO:2 or 3 comprising a reversible modification that increases its bioavailability and facilitates its permeation through the blood brain barrier and epithelia tissue. The specification indicates the peptide of the invention may undergo reversible chemical modification such

as esterification of the carboxyl group of Glu or Asp residue in the peptide to increase its bioavailability and to facilitate its permeation through the blood brain barrier and epithelia tissue, and the esterification is reversible because the ester bond is recognized by intracellular esterases which hydrolyze it (page 5, lines 14-23). However, the specification does not provide sufficient teachings to enable the full scope of the claim as discussed in the stated rejection. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breadth of the claims, the absence or presence of working examples, the state of the prior art and relative skill of those in the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breadth of the claims:

The breadth of the claims is broad and encompasses unspecified variants regarding the reversible modification and the identity of the group being modified, which are not adequately described or demonstrated in the specification.

(2). The presence or absence of working examples:

The specification has indicated the peptide of the invention may undergo reversible chemical modification such as esterification of the carboxyl group of Glu or Asp residue. However, there are not other reversible modifications being identified and demonstrated.

(3). The state of the prior art and relative skill of those in the art:

Esterification of the carboxyl group of Asp or Glu in the peptide is known to increase the hydrophobicity of the peptide. However, the general knowledge and level of

the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on the identities and effects of the modified peptides to be considered enabling for variants.

(4). Predictability or unpredictability of the art:

The claim encompasses many reversible modifications for the peptide, however, the identities of groups in the peptide having reversible modifications, and the effects of modified peptides are not sufficiently described in the specification, and the invention is unpredictable regarding the effect of the modified peptide in increasing its bioavailability and facilitating its permeation through the blood brain barrier and epithelia tissue.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary.

The claim is directed to a peptide having an amino acid sequence of SEQ ID NO:2 or 3 comprising a reversible modification that increases its bioavailability and facilitates its permeation through the blood brain barrier and epithelia tissue. The specification indicates the peptide may undergo reversible chemical modification such as esterification of the carboxyl group of Glu or Asp residue in the peptide to increase its bioavailability and to facilitate its permeation through the blood brain barrier and epithelia tissue (page 5, lines 14-23). However, the specification has not demonstrated various reversible modifications of the peptide, nor has shown the effects of the modified peptides. Moreover, there are no working examples indicating the claimed variants except the esterification of the Glu or Asp. Since the specification does not provide sufficient teachings on the reversible modifications of the peptide, it is necessary to have

additional guidance to carry out further experimentation to assess the effect of the peptide having various reversible modifications.

(6). Nature of the Invention

The scope of the claim includes the peptides having various reversible modifications, however, the specification has not provided sufficient teachings regarding the modified peptide and its effect in increasing its bioavailability and facilitating its permeation through the blood brain barrier and epithelia tissue. Thus, the disclosure is not enabling for reasons discussed above.

In summary, the scope of the claim is broad, while the working example does not demonstrate the claimed variants, the teachings in the specification are limited, and the effects of the modified peptides are unpredictable, therefore, it is necessary to have additional guidance and to carry out further experimentation to assess the effect of the modified peptide in increasing its bioavailability.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 2 and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claim 2 is indefinite because the claim cites "the amino acids of said peptide are D-amino acids", which does not conform the limitation of SEQ ID NO:2 or SEQ ID NO:3, i.e., the amino acids in the sequence are L-amino acids.

9. Claim 15 is indefinite because the claim lacks an essential step in the method of treating face wrinkles and facial asymmetry. The missing step is the outcome of the treatment. Claim 15 is also indefinite because of the use of the term "and/or". The term "and/or" renders the claim indefinite, it is unclear whether the limitation after "and/or" is included or not, and if included is to be read as an alternative "or" or the conjunctive "and". The word "wrinkels" is misspelled.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Montal *et al.* (WO 97/34620).

Montal *et al.* teach the amino acid sequence of SNAP-25 (Fig. 3, SEQ ID NO:1 of the WO document), which contains SEQ ID NO:2 or 3 (claim 1 and 2). The claims are anticipated by the reference because claim 1 cites a peptide "having" an amino acid sequence of SEQ ID NO:2 or 3, which reads as a peptide "comprising" an amino acid sequence of SEQ ID NO:2 or 3.

***Conclusion***

11. Claims 1-5, 11, 12 and 15 are rejected, and claims 13, 14, 16-19 and 23 are objected to.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. CMK
Patent Examiner

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March 17, 2004

ROBERT A. WAX
PRIMARY EXAMINER